THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI – TAMILNADU.

DISSERTATION
ON

PROGNOSTIC IMPORTANCE OF

HYPONATREMIA IN

ACUTE ST-ELEVATION MYOCARDIAL INFARCTION

SUBMITTED FOR M.D. DEGREE EXAMINATION
BRANCH I
(GENERAL MEDICINE)

EXAMINATION
IN
September – 2006

THANJAVUR MEDICAL COLLEGE
THANJAVUR

CERTIFICATE

This is to certify that this dissertation entitled ***"SHORT TERM PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION"*** is the bonafide record work done by **Dr. V. SADEESH KUMAR,** submitted as partial fulfillment for the requirements of M.D. Degree Examinations, Branch I (General Medicine) to be held in September 2006.

Prof. Dr. K. GANDHI, M.D.,
Unit chief ,
Professor & Head of the Department,
Department of General Medicine,
Thanjavur Medical College, **Thanjavur**

Dean,
Thanjavur medical college,
Thanjavur

ACKNOWLEDGEMENTS

I am immensely grateful to my unit chief, Professor and Head of the Department medicine, **Prof. DR. K GANDHI M.D.**, for his valuable support and encouragement throughout this study

I express my he artful thanks to our former Dean Dr. K. Kalaiselvi M.D. , for permitting to under take and complete this dissertation in this medical college , Thanjavur

I also thankful to the unit chiefs Dr. S. Balakrishnan M.D., Dr.Jeeva M.D., Dr.Ramasamy M. D., for having permitted me to work upon the patients who were admitted in their units during my study.

My sincere and thankful gratitude to Prof. Dr. N. Senguttuvan M.D., D.M. professor and H.O.D. of cardiology department for his guidance.

I am extremely thankful to my beloved Assistant professors of Medicine Dr.P.Krishnamurthy M.D., Dr.A.Rajendran M.D., for their constant encouragements and help through out this dissertation work

I extend my heartful thanks to Dr.G.Senthil kumar M.D., D.M., Assistant professor, Cardiology department, DR.G. Kannappan M.D., Assistant Professor of Medicine for their guidance and cooperation throughout the study.

I thankful to all the staffs of the department of BIOCHEMISTRY for their help to complete this study successfully.

I will not be pardoned if I am not thankful to the patients who have participated in this dissertation with out whom the study would not have been possible.

I owe this dissertation to my family members and friends for moral support and timely help without which could not have completed this dissertation work.

Finally I owe my thanks to THE ALMIGHTY for the successful completion of the study.

CONTENTS

INTRODUCTION

In 1950, the Eighth Edition of the Price Textbook of Medicine, outlining the management of patients with Acute Myocardial Infarction, stated that "taking cases as a whole, it would appear that somewhat more than half survive the acute attack. The first week is particularly dangerous, especially the first two or three days, and prognosis must be very guarded at least three months of complete rest, followed by a period of partial rest is strongly indicated"[1] Retrospectively, this cautionary approach may seem exaggerated, but it must be remembered that until 1912, it was believed that acute myocardial infarction was uniformly fatal. It was James Herrick, a Chicago physician, who first described survival after infarction in an article that appeared in the Journal of the American Medical Association in 1912.[2]

In subsequent years, as the understanding of the pathophysiological principles of myocardial infarction began to grow, treatment came to be based on sounder tenets, and the prognosis began to improve. Substantial advances in the treatment of acute myocardial infarction (MI) have occurred over the past several years as a result of important observations in basic myocardial research and through the vital evaluative mechanism of randomized clinical trials.[3-12]

A steady decline in the mortality rate from STEMI has been observed across several population groups since 1960[13]. Several phases in the management of patients have contributed to the decline in mortality from STEMI.

The **“clinical observation phase”** of coronary care consumed the first half of the 20-th century and focused on a detailed recording of physical and laboratory findings, whereas treatment consisted of strict bed rest and sedation Subsequently the **“coronary care unit phase”** began in the mid 1960s and was notable for detailed analysis and vigorous management of cardiac arrhythmias. Killip and Kimball published their seminal article titled ‘The treatment of Myocardial Infarction in a Coronary Care Unit -- A Two Year Experience with 250 Patients’ in the Lancet in 1967. Here they espoused the guidelines for the setting up of such units, and showed conclusively that intensive treatment, especially of arrythmias, produced striking improvement in the mortality. This article also expounded the now famous Killip classification.[14]

The **“high technology phase”** was ushered in by the introduction of the pulmonary artery balloon flotation catheter, setting the stage for bedside hemodynamic monitoring and more precise management of heart failure and cardiogenic shock associated with STEMI. A battery of tests, sometimes providing overlapping information, was developed during the high technology phase. The

modern **"reperfusion era"** of coronary care was introduced by intracoronary and then intravenous fibrinolysis increased use of aspirin, and development of primary percutancous coronary intervention (PCI).

Several of these options -- which include angioplasty, intra-coronary stenting, intra-coronary brachytherapy, rotablation techniques, bypass grafting and transmyocardial laser revascularisation are potentially life-threatening. Given this scenario, it becomes important for the physician to have techniques to identify, with reasonable accuracy, those patients at highest risk for developing harmful events, in whom such aggressive intervention may be advisable despite the risks. Despite therapeutic advances, recent large-scale randomized clinical trials report 6% to 9% early mortality rates (30 to 35 days), even for patients receiving thrombolytic therapy within 6 hours of symptom onset [15-18]

Yet another problem, faced by third-world physicians in particular, is that in several hospitals, the coronary care facilities are severely limited compared to the number of needy patients. Thus, a system of prognostication is needed in this scenario to choose between patients and to identify the poor-prognosis group that may have maximum benefit from intensive care. Prognostication in Acute

Myocardial Infarction has evolved over the years. Today, a distinction is made between short-term or in-hospital prognosis and long-term prognosis. Various workers in the field have attempted to shift through the multitude of factors affecting prognosis.

LIMITATIONS OF CURRENT THERAPY

Despite the gratifying success of medical therapy for STEMI, several observations indicate that considerable room for improvement exists. The short-term mortality rate of patients with STEMI who receive aggressive pharmacological reperfusion therapy as part of a randomized trial is in the range of 6.5 to 7.0 percent, [19] whereas observational data bases suggest that the mortality rate in STEMI patients in the community is 15 to 20 percent. [20] In part, this difference relates to the selection of patients without serious comorbidities for clinical trials.

Often, choices among alternative therapies or decisions regarding the allocation of clinical resources are based on an assessment of patient risk. Careful attention to pivotal factors that increase the risk of early mortality might illuminate the role of second-tier interventions or adjunctive pharmacotherapeutics that would further lower the fatality rate of acute MI.

To be broadly useful, a risk-assessment algorithm should include all clinically relevant prognostic indicators and should be derived from a population that represents the types of patients seen in clinical practice so that stable estimates of true risk relations can be assessed. A useful model should appropriately weight clinically relevant predictors and be validated in a population with a broad spectrum of patients and hospital settings, in which risk profiles may soon be required. Though many studies have attempted to define the prognosis of patients with MI and/or provide risk algorithms, [21-29] they were performed before the widespread use of thrombolytic agents [15- 19] or were limited in sample size, diversity of medical care systems, or spectrum of clinical data.

In this study, an attempt has been made to apply prognostic factors cited in the literature in the setting of a teaching hospital situated in predominantly rural surroundings. Our institution regularly faces a demand for intensive cardiac care well out of proportion to the available facilities -- hence such a study is especially significant in our context. Only those described factors that are easily available in such a setting have been selected for the purposes of the study. The attempt has been to identify the factors that will help the attending physician to reasonably identify those patients at highest risk of short-term mortality so that the relatively scarce resources can be allotted in the most efficient and beneficial manners possible.

AIMS OF THE STUDY

1. To determine the prevalence and prognostic implications of hyponatremia in the setting of acute ST-elevation myocardial infarction.

2. To validate the accuracy of frequently used prognostic index killip classification.

3. To investigate the relative importance of other prognostic factors cited in the literature.

4. To calculate the statistical associations between such characteristics and short-term prognosis.

REVIEW OF LITERATURE

REVISED DEFINITION OF MYOCARDIAL INFARCTION(MI)[30]

Criteria for acute, evolving, or recent MI

Either one of the following criteria satisfies the diagnosis for an acute, evolving, or recent MI :-

1. Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:

   a. Ischemic symptoms
   b. Development of pathologic Q waves on the ECG reading
   c. ECG changes indicative of ischemia (ST-segment elevation or depression).
   d. Coronary artery intervention (e.g., coronary angioplasty)

2. Pathological findings of an acute MI

Criteria for established MI

Either of the following criteria satisfies the diagnosis for established MI :

1. Development of new pathological Q waves on serial ECG readings. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.

2. Pathological findings of a healed or healing MI.

Several researchers all over the world have been attempting for decades to establish those criteria that best define patients with a poorer prognosis. Taken in toto, the various studies and articles published in the literature may be classified conveniently into two major headings:-

1. Criteria obtained at the initial physician contact -- including patient characteristics (e.g., age, gender), details of history, the initial clinical examination findings.

2. The laboratory parameters obtained on admission.

CHEST PAIN

Despite the recent advances in the laboratory diagnosis of Acute Myocardial Infarction (AMI), the history remains of substantial value in arriving at a diagnosis. A prodrome of chest discomfort can usually be elicited in 20 to 60% of patients with AMI.[31]

The pain of AMI resembles that of classic angina pectoris, except that it is more severe, occurs at rest or with lesser activity than usual, lasts longer (more than 30 minutes), is associated with more systemic symptoms (e.g., diaphoresis, nausea), and is not relieved by rest or nitrates.

The essence in the management of AMI today is ‘speed’. Patients who are hospitalised and treated earlier (especially with thrombolysis) have a better prognosis. Hence, all factors that lead to a delay in diagnosis and treatment, especially the absence of chest pain or atypical presentations entail a poor prognosis.

In an analysis of the atypical presentations of AMI, Bean et. al., lists the following :- [32]

1. Congestive heart failure
2. Classic angina pectoris (not severe or prolonged)
3. Atypical locations of the pain
4. Central nervous system manifestations, resulting from a reduced cardiac output, resembling a stroke.
5. Apprehension and nervousness
6. Sudden mania and psychosis
7. Syncope

8. Overwhelming weakness
9. Acute indigestion, and
10. Peripheral embolism.

To this list must be added those patients with “silent” AMI -- who have had no symptoms at onset. Such presentations are commoner in diabetics and hypertensives, and both of these conditions are also associated with an increased mortality.[33]

TIME SINCE ONSET OF SYMPTOMS

Studies involving large numbers of patients have revealed wide variations in the time elapsed between symptom onset and arrival at the hospital. Researchers have investigated for a relationship between this delay and inhospital mortality. However, there are certain complexities in this relationship, as follows :-

Most sudden deaths in AMI occur due to ventricular arrythmias, and this risk is maximum in the first hour after symptom onset.[34] With each subsequent hour, the risk decreases, giving rise to the paradoxical situation where a patient who presents late to the hospital has a lesser risk of sudden death than one who presents early for treatment. 40 to 60% of patients have some degree of left ventricular (LV)

dysfunction at presentation , if untreated, this may go on to cardiogenic shock, the commonest cause of in-hospital death in AMI.[35] This implies that the patient who presents sufficiently early for shock to be treated or prevented has a better prognosis.

Established beyond reasonable doubt that the patient who presents early enough for thrombolysis has large benefits from reperfusion, vastly improving the prognosis.[36]

THE CONCEPT OF "DOOR-TO-NEEDLE" TIME

The term door-to-needle time was coinned to figuratively describe the time elapsed between the patient's symptom onset upto the actual intravenous infusion of the thrombolytic agent. This includes all the delays involved in contacting a doctor, referral to an ICCU, obtaining transport, and the time spent in the emergency room or casualty of the hospital before reaching the ICCU.

Raitt et. al., have shown that each 30 minute delay is associated with a 1% increase in infarct size.[37] Julian D.G., analysing the results of five mortality trials, concluded that gaining about one hour prior to thrombolysis decreases mortality by about 17%.[38] Even for patients presenting later than this 'window' period of 6 hours, thrombolysis can be beneficial, compared to those that do not receive

such treatment. Yusuf et. al., showed a 22% reduction in mortality for those treated at 12 -- 24 hours. The ISIS-2 trial extended the concept of beneficial late perfusion with its results revealing a significant benefit beyond 6 - 12 hours, and even 12 - 24 hours.[36] These findings are confirmed by the ISIS-3 and EMERAS trials. The newer agents such as t-PA, Urokinase, or even emergency coronary angioplasty may achieve better late reperfusion than streptokinase.[39]

AGE OF THE PATIENT

It has long been appreciated that the mortality in AMI is increased in those over 60 years of age[49]. Several studies have documented a greater incidence of congestive failure, malignant arrythmias and sudden death in this group . Although the survival of elderly patients (>65 years of age) after STEMI has improved significantly, advanced age consistently emerges as one of the principal determinants of mortality in patients with STEMI.[40]

The effects of aging on the heart have been well studied.[31] The aging heart has a poorer ability to respond to the ischemic insult, especially since the remaining perfused areas have a diminished functional reserve. Co-existent diseases, prior myocardial damage and larger infarcts are all commoner in the elderly.[31]

Since age has been considered a relative contraindication, the benefits of thrombolytic therapy have not been as dramatic in the lderly. In addition, older patients are more likely to present later (increased collaterals or autonomic neuropathy), or have other contraindications to thrombolysis.[40]

GENDER -- RELATED DIFFERENCES IN PROGNOSIS

Unlike in previous years, the incidence of AMI in women is increasing. AMI in women has certain peculiarities. Women are mostly older than men at presentation and are more likely to have atypical pain. Hypertension, diabetes, unstable angina, hyperlipidemia, congestive cardiac failure or silent infarctions are all commoner in women. Women more frequently have non-Q AMI and tend to present later to hospital.[41] Of interest, after STEMI, younger women but not older women have higher rates of in-hospital mortality than men of the same age.[41]

The more serious presentations -- rales, hypotension, heart block or tachycardia are commoner in women. It has been noted that diabetes dramatically increases the mortality among women > 65.[41]
The pathogenic mechanisms different in women include : [42]

- a greater incidence of vasospastic and microcirculatory angina,

- different plaque components (more cellular and fibrous tissue)
- different endothelial tone due to hormonal influences
- different hemostasis (higher fibrinogen and factor VIII levels.)

PREVIOUS HISTORY OF CORONARY HEART DISEASE

A preceding history of coronary artery disease can have varying effects on the short-term prognosis.[33] Patients with a second infarction are more likely to die than those who suffer at first. This finding, confirmed in most studies, probably reflects the importance of the extent of viability of remaining myocardium versus infarcted myocardium in determining the prognosis. In all age groups and in both sexes, history of heart failure is associated with a poorer outcome, with an increased mortality of 10 to 15% as the NYHA functional class increased from I to IV.[43]

DIABETES AND ITS EFFECT ON PROGNOSIS

Diabetes Mellitus is an important risk factor for the development of coronary heart disease. The early pioneering studies on AMI, especially those by Killip and Norris suggested that the presence of diabetes had a significant effect on the mortality. The famous Framingham Heart Study indicated that diabetes increased the risk of death in women, but not men, after a first AMI.[14] They tend to have larger infarcts, and show a greater incidence of shock, cardiac failure and metabolic problems.[44]

Hyperglycemia and impaired glucose tolerance are common in patients with STEMI. Although the absolute levels of blood insulin are often in the normal range, they are usually inappropriately low for the level of blood sugar, and there may be relative insulin resistance as well. Patients with cardiogenic shock often demonstrate marked hyperglycemia and depressed levels of circulating insulin, often with complete suppression of insulin secretion in response to tolbutamide. These abnormalities in insulin secretion and the resultant impaired glucose tolerance appear to be secondary to a reduction in pancreatic blood flow as a consequence of splanchnic vasoconstriction accompanying severe left ventricular failure. In addition, increased activity of the sympathetic nervous system with augmented circulating

catecholamines inhibits insulin secretion and augments glycogenolysis, also contributing to the elevation of blood sugar.[45]

Glucose appears to be a more favourable energy source than free fatty acids for the ischemic myocardium by more efficiently replenishing the Krebs cycle and stimulating contractile performance.[46] Because hypoxic heart muscle derives a considerable portion of its energy from the metabolism of glucose and because insulin is essential for the uptake of glucose by the myocardium as well as for myocardial protein synthesis and inhibition of lysosomal activity, the deleterious effects of insulin deficiency are clear. These metabolic considerations, combined with epidemiological observations that diabetic patients have a markedly worse prognosis, have served as the foundation for efforts to more aggressively administer insulin-glucose infusions to diabetic patients with STEMI.

To compound matters further, the increased adrenergic discharge at the time of AMI worsens insulin resistance, thus impairing myocardial glycolysis. The concentration of circulating free fatty acids rises, and this can predispose to the development of malignant ventricular arrhythmias.[31]

HYPERTENSION AND ITS EFFECT ON PROGNOSIS

The GISSI-2 trial, one of the largest ever series of AMI patients, (11,483 patients, of which 3306 were hypertensive) investigated the prognostic value of hypertension in those receiving thrombolysis. Their results show a significantly higher mortality for hypertensives, both in-hospital and at 6 months. LV failure and recurrent ischemic events were also more common among hypertensives.[47]

PULSE, BLOOD PRESSURE AND HEMODYNAMIC STATUS AT ADMISSION

Despite the tremendous advances in the management of AMI, the initial clinical examination remains the basic foundation upon which all subsequent steps are planned. It has even been observed that the initial judgment regarding prognosis by the admitting doctor, based on the initial clinical examination correlates well with the outcome.[48] Based on the admission pulse rate, several judgments can be made. Most commonly, the pulse is initially rapid (100 to 110 / minute) and regular, slowing considerably when the patient's pain and anxiety are relieved. Sinus tachycardia lasting for more than

24 hours carries a poor prognosis.[31] Heart rate at entry displayed a significant U-shaped relation, with elevated mortality at very low and at high heart rates [49]. Previous studies have identified sinus tachycardia as a indipendent prognostic factor [50].

The majority of patients with AMI are normotensive, although the associated tachycardia may reduce the systolic pressure and narrow the pulse pressure. While previously normotensive patients may show a hypertensive response due to sympathetic activity, patients with hypertension may become normotensive owing to the acute circulatory disturbances. A strong prognostic relation was also present for systolic blood pressure, notably in the range below 120 mm Hg. A similar but less significant pattern existed for diastolic blood pressure [49].

The SPRINT study group, reporting in October 1995, found an increasing mortality with increasing heart rates at admission, from less than 70 to more than 90 / minute. At even higher heart rates, the increasing trend of mortality was confined to those with heart failure. A combination of a rate more than 90 with a systolic pressure less than 120 mm of Hg was a powerful predictor of in-hospital mortality.[51]

In patients with AMI, heart failure is characterised by either distolic dysfunction (pulmonary congestion or venous

hypertension) or both diastolic and systolic (decreased cardiac output and ejection fraction). Clinical manifestations become more obvious as the extent of injury increases and thus they carry an adverse prognosis. These factors have been best quantified by the Killip classification, which groups patients into four classes with increasing signs of failure carrying higher degrees of mortality.[14]

Patients develop cardiogenic shock when more than 40% of the myocardium is destroyed. Beyond the immediate phase, cardiogenic shock is the commonest cause of mortality. The defining characteristics of this condition includes :-

- evidence of hypoperfusion (cold, clammy skin, impaired mentation, oliguria)
- systolic BP less than 80 to 90 mm of Hg
- LVEDP or PCWP more than 18 mm of Hg.
- cardiac index less than 1.8 mL/min/m^2
- evidence of primary cardiac abnormality.

The hospital mortality for cardiogenic shock is in the region of 60 - 80%. The incidence of ventricular arrhythmias and heart block was found to be higher in these patients (Killip et. al.)[14] . By multivariate analysis of their cohort of 845 patients, Hands et. al.,

found that the predictors of cardiogenic shock included age > 65, ejection fraction < 35% peak CK-MB value more than 160 IU/L., and a history of diabetes or prior infarction.[52]

LEUCOCYTE COUNT AND PROGNOSIS

An increase in the white cell count occurs frequently following an AMI. This may be a reaction to tissue necrosis, or be the effect of released catecholamines, or both. The elevation starts 2 hours after onset, reaches a peak at 2 to 4 days, and usually ranges from 12-15, 000 per cu.mm., but can occasionally rise upto 20,000. Often there is a polymorphonuclear leukocytosis, and a shift tot he left, with band forms seen [53,54]. The ESR and the PCV may also show transient rises.

A study by Furman et.al., concluded that the peripheral blood WBC count correlated directly with short-term prognosis. This was independent of other factors such as the site or size of the infarction.[55]

Yet another study by Petrov et. al., also found that a leucocytosis grater than 19,000/cu.mm. was seen in all patients of AMI in his series who expired in hospital. He suggests that

a count greater than 15,000 is an important prognostic sign for the final outcome of AMI.[56]

ADMISSION HYPERGLYCEMIA AND PROGNOSIS

Hyperglycemia, inappropriate insulin levels and impaired glucose tolerance are common in patients with AMI. Hyperglycemia, even without previous diabetes, is associated with a high mortality and a higher incidence of failure.[57] Patients with cardiogenic shock often show marked hyperglycemia and low levels of circulating insulin.[58]

These abnormalities are in part due to a reduction in pancreatic blood flow,this is a consequence of intense splanchnic vasoconstriction which accompanies severe heart failure. In addition, increased sympathetic activity during AMI increases catecholamines, inhibits insulin secretion and augments glycogenolysis, all leading to hyperglycemia.[31]

Hypoxic heart muscle derives a considerable portion of its energy from the metabolism of glucose, and since insulin is essential for its uptake here, a deficiency of or resistance to insulin has deleterious effects.

HYPONATREMIA

Hyponatremia, defined as a plasma sodium level <135mmol/l (<135mEq/L). Hyponatremia is a common electrolyte disorder among hospitalized patients [59], especially in the postoperative period [60] and in patients with heart failure, nephrotic syndrome, or cirrhosis [61,62]. It is recognized as a predictor of adverse outcomes in hospitalized patients, and its prognostic implications are usually attributed to the severity of the underlying condition [59,63]. The prevalence of hyponatremia in hospitalised patients is 2%[64]. Hyponatremia can be associated with low, normal, or high tonicity. [65,66]

Effective osmolality or tonicity refers to the contribution to osmolality of solutes, such as sodium and glucose, that cannot move freely across cell membranes, thereby inducing transcellular shifts in water.[67] Dilutional hyponatremia, by far the most common form of the disorder, is caused by water retention. If water intake exceeds the capacity of the kidneys to excrete water, dilution of body solutes results, causing hypo osmolality and hypotonicity (Fig. B, E, F,andG) Hypotonicity, in turn, can lead to cerebral edema, a potentially life threatening complication.[68] Hypotonic hyponatremia can be associated, however, with normal or even high serum osmolality if sufficient

amounts of solutes that can permeate cell membranes (e.g., urea and ethanol) have been retained (Fig. C). Importantly, patients who have hypotonic hyponatremia but normal or high serum osmolality are as subject to the risks of hypotonicity as are patients with hypo-osmolar hyponatremia.

The nonhypotonic hyponatremias are hypertonic (or translocational) hyponatremia and isotonic hyponatremia.[65,66] Translocational hyponatremia results from a shift of water from cells to the extracellular fluid that is driven by solutes confined in the extracellular compartment (as occurs with hyperglycemia or retention of hypertonic mannitol); serum osmolality is increased, as is tonicity, the latter causing dehydration of cells (Fig.D). Retention in the extracellular space of large volumes of isotonic fluids that do not contain sodium (e.g., mannitol) generates iso-osmolar and isotonic hypontremia but no transcellular shifts of water.

A common clinical problem, hyponatremia frequently develops in hospitalized patients. Although morbidity varies widely in severity, serious complications can arise from the disorder itself as well as from errors in management.

Suxon LA, found that serum sodium ≤ 134 mEq/liter, is a independent predictor of hemodynamic deterioration in advanced heart failure.[70]

Hyponatremia has been shown to be a predictor of cardiovascular mortality among patients with heart failure [69,70]

MECHANISM OF HYPONATREMIA IN HEART FAILURE

Heart Failure is a complex clinical syndrome that is growing in maganitude as the population ages. It is difficult to define but relatively strightforward to diagnose. Heart failure implice underlying structural and functional changes in heart that contribute importantly to the clinical syndrome. There is no single cause are unifying mechanism in heart failure[71].

In the presence of heart failure several mechanism promote the development of hyponatremia. Vasopressin is essential to the development of hyponatremia because atleast fifteen liters of fluid can be excreted daily when Vasopressin is appropriately inhibited [72]

Hypoosmolarity which inhibits the release of vasopressin in healthy subjects is associated with persistently high plasma concentration of vasopressin in heart failure [69].

The hyponatremia is due in part to nonosmotic release of AVP, which acts on the kidney to reduce free water clearance. Release of AVP in heart failure probably occurs via activation of carotid baroreceptors [73]. Plasma AVP levels are often but not always increased in patients with LV dysfunction [74] and heart failure.[75] AVP acts on the V_2 receptors in the collecting duct of the kidney via adenylate cyclase to translocate aquaporin-2 water channels from cytoplasmic vesicles to the apical surface of the collecting duct. AVP also increases aquaporin-2 channel synthesis.Activation of V_1 receptors in vascular tissue contributes to heightened vascular resistance and myocardial dysfunction in heart failure.[76]

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM

The RAAS plays an important role in the pathogenesis of heart failure , and consistent benefit has been derived from ACE-inhibitor therapy in patients with heart failure. The mechanismsresponsible for the release of renin from the renal cortex have been exhaustively studied [77] and include sympathetic drive to the kidneys, hyponatremic perfusate to the macula densa of the kidney, and use of diuretics and a

low-sodium diet, which tends to promote a relative volume contraction. Renin proteolytic enzyme has little biologic activity, but it interacts with angiotensinogen to split off two amino acids to form angiotensin I, which is then cleaved by ACE, which is distributed widely in the vascular system, especially the lungs, to produce angiotensin II, a peptide with a vast range of biological activities. Angiotensin II in turn stimulates release of aldosterone from the adrenal cortex, which also has an array of biological effects, including sodium and water retention, kaliuresis, and enhanced collagen turnover and organ remodeling.

Activation of carotid baroreceptors has been implicated in the nonosmotic release of vasopressin due to arterial underfilling [61,62,78]. In addition, increased expression of messenger RNA for vasopressin in the hypothalamus has been described in animal models [79]. Moreover, the renal effect of vasopressin is enhanced in heart failure. The mechanisms leading to hyponatremia in heart failure may be responsible in part for the adverse prognosis associated with hyponatremia.

MECHANISM OF HYPONATREMIA IN ACUTE MI

It is not clear whether the mechanisms that contribute to the development of chronic hyponatremia are involved in our study. For

example, increased hypothalamic expression of vasopressin [79] and upregulation of water channels in the collecting duct [80] require several weeks of heart failure to develop. In the setting of acute myocardial infarction, hyponatremia on admission or a rapid reduction in plasma sodium level occurs in a substantial number of patients. In addition, hyponatremia remained an independent predictor of mortality even after adjustment for the most important clinical and hemodynamic covariates that determine prognosis in ST-elevation myocardial infarction [81,82,83].

In acute myocardial infarction, nonosmotic release of vasopressin may occur due to the acute development of left ventricular dysfunction, in response to pain, nausea, and major stress, the most common mechanisms of hyponatremia in adults; or in response to the administration of analgesics and diuretics [84,85]. In this setting, vasopressin levels increase concomitantly with the activation of other neurohormones such as renin and norepinephrine [86]. However, vasopressin level does not correlate with serum osmolarity in myocardial infarction [86], suggesting that nonosmotic mechanisms are involved.

LOCAL MYOCARDIAL AND SYSTEMIC RENIN ANGIOTENSIN SYSTEM

Noninfarcted regions of the myocardium appear to exhibit activation of the tissue renin-angiotensin system with increased angiotensin II production. Both locally and systemically generated angiotensin II can stimulate the production of various growth factors, such as platelet-derived growth factor and transforming growth factor, that promote compensatory hypertrophy in the noninfarcted myocardium as well as control the structure and tone of the infarction process include release of endothelin, PAI-1, and aldosterone, which may cause vasoconstriction, impaired fibrinolysis, and increased socium retention, respectively. Inhibition of generation of circulating and tissue angiotensin II is one of the proposed mechanisms of benefit from ACE inhibitors in STEMI.

In patients with myocardial infarction, hyponatremia may be aggravated further by the concomitant activation of the renin-angiotensin system and increased catecholamine production [87,88]. These factors decrease the glomerular filtration rate and subsequent delivery of tubular fluid to the diluting segment of the nephron, further contributing to decreased renal water excretion [90]. Indeed, the degree

of neurohormonal activation correlates with the severity of hyponatremia in patients with chronic heart failure [89].

BNP levels may be a marker of the degree of left ventricular dysfunction in patients with STEMI and that markedly elevated levels of BNP correlate with a worse prognosis.[91,92,93]

ADRENAL CORTEX

Plasma and urinary 17-hydroxycorticosteroids and ketosteroids, as well as aldosterone, are also markedly elevated in patients with STEMI. The magnitude of the elevation of cortisol correlates with infarct size and mortality. Glucocorticosteroids also contribute to the impairment of glucose tolerance[13].

ECHOCARDIOGRAPHY AND PROGNOSIS AFTER AMI

The ease of use of Echocardiography, portability, and lack of radiation or other biologic hazards make it an ideal investigation in critically ill patients. It enables estimation of cardiac function and wall motion abnormalities.[94]

Patients with normal ejection fraction (EF) by Echo have been shown to have essentially no mortality or complications in hospital. The mortality was 2% with an EF >35% and 37% if <35%. A recent study suggests that LV endsystolic volume may be an even more sensitive index than the ejection fraction.[94]

Objective evaluation is also done by scoring the wall motion index (normally = 1). Peels et. al., have proven the prognostic value of the wall motion score index (WMSI). Kober et. al., found an association between a WMSI of >1.6 and failure/death.[95]

Echo can also assess the area of dyskinesis, and show expansion of infarcted area , thus predicting the prognosis. It can also show the success of reperfusion therapy as an increasing WMSI. It can be used to confirm the presence of complications that worsen the outcome. Doppler evaluation of mitral and peak aortic flow rates have also been used for prognosis, and they have been found to correlate well with pulmonary capillary wedge pressure.[96]

MATERIALS AND METHODS

This study was conducted in the Thanjavur Medical College Hospital, Thanjavur, during the period of September, 2005 to March, 2006.

STUDY POPULATION

A total of 54 patients admitted to the Intensive Cardiac Care Unit were studied. There were 40 male and 14 female patients, ranging from 35 years to 85 years. Average age of presentation 54.7 years.

CRITERIA FOR ENTRY INTO THE STUDY

Patients with a diagnosis of Acute Myocardial Infarction (AMI) were entered into the study. A definitive diagnosis of AMI was made if the patients satisfied the following criteria **:-**

i)A history of typical chest discomfort, lasting for more than thirty minutes, not relieved by rest or nitrates.

ii) Typical ECG changes of AMI (Q waves or ST/T wave changes in two contiguous leads, or the appearance of new left bundle branch block).

EXCLUSION CRITERIA

i) Patients with elevated renal parameters.

ii) Very late presentation more than 72 hours.

VARIABLES RECORDED AT ADMISSION

Routine history taking, physical examination and laboratory investigations were performed in all subjects. The variables recorded specifically for the purposes of this study were as follows **:-**

i) Presenting History :

- duration of chest discomfort
- associated symptoms
- time of onset of symptoms
- triggering factors, if any

ii) Previous History :

- previous infarction or angina
- diabetes mellitus
- hypertension
- other cardiovascular diseases
- symptoms of cardiac failure
- use of tobacco and alcohol
- Contraindications to thrombolytic thereby (recent surgery / trauma / bleeding / cardiopulmonary resuscitation / CNS diseases).

iii) Clinical Examination :

Special emphasis was placed on recording :-

- admission heart rate
- admission blood pressure
- signs of cardiac failure (including highest level on the chest wall where crepitations of cardiac failure, if any, are heard).
- signs of hypoperfusion

iv) Admission Electrocardiogram (ECG) :

(a) Site of infarction : anterior, inferior, lateral, right ventricular, or combinations of these.

The sites were defined as follows :-

- Anterior : Changes in VI to V4
- Inferior : Changes in II, III, aVF
- Lateral : Changes in V5, V6, I or aVL
- Right ventricular : ST rise in V4R > V2

(b) Number of leads with

i. Q waves and

ii. ST elevation.

(v) Laboratory Investigation

- total WBC count
- blood sugar at the time of admission, 24, 48, 72 Hours
- Serum Sodium on admission, 24, 48,72 Hours

Levels were corrected at each time, point based on the assumption that plasma sodium concentration should fall by 1.6 mmol/L for every 100-mg/dL rise in plasma glucose concentrations [100,101]. Thus, for

every 100mg/dL increase in plasma glucose concentration above 100 mg/dL, 1.6 mmol/L was added to the plasma sodium concentration.

- Serum Pottasium on admission, 24, 48,72 Hours
- Haemoglobin on admission,
- Blood Urea, Serum Creatinine

are measured.

Qualifying patients received thrombolytic therapy with 1.5 million units of streptokinase, followed by heparin for 5 to 7 days.

Assessment of left ventricular ejection fraction by echocardiography was performed either on day 4 or 5 of hospitalization in most patients or earlier if clinically indicated.

DISCUSSION

A 54 patients in this study were all chosen with strict adherence to the entry criteria. Most patients arrived at the hospital without prior referrence by Doctor. Though some study have reported a difference in mortality depending on the qualification of referring Doctor.Our referred cases were too few in number to arrive such a conclusion. 30% of patients are only referred by private practitioners.

In our study the overall mortality rate within 30 days is 12.9% Kerry L.Lee., found that mortality rate within 30 days is 7% in his study, among them 39% died within 24 hours. Alexander Goldberg found 10% mortality within 30 days following MI.

Many studies report the commonest location of MI is anterior infarction, as in our study (27 out of 54 patients). Mortality was also higher in patients with anterior infarction compared to inferior infarction (85.7% Vs. 14.3%). Multiple previous studies have reported that patients with anterior infarction have the highest risk of death[102.103], and isolated inferior infarction has been associated with the lowest risk.

An increasing age has been found to worsen prognosis both in terms of likelyhood of death and in the development of life threatening complications [83] Age over 60 significantly increasing mortality compared to those less than 60 years. The relation was relatively flat until age 60, after which the risk of death accelerated dramatically.

In our study the percentage of mortality in males is more than females. Kerry L.Lee., found female sex was only a marginally independent Prognostic factor (P=0.043) in his study[49].

HYPONATREMIA

In our study hyponatremia was present in 10 out of 54 patients. It comes to 18.5%. Comparing to Goldberg et. al., this is 5.6% higher than what he found. None of them presented with hyponatremia receive prior diuretic therapy. Among hyponatremia on admission the mortality rate is 30%. Goldberg et. al., found 19.9% mortality in hyponatremic patients on admission [97].

In a study of 235 patients admitted to a coronary care unit in the prethrombolytic era (of whom 190 were subsequently diagnosed with acute myocardial infarction), Flear et. al., found higher in-hospital

mortality rates among patients with minimal plasma sodium levels ≤ 130 mmol/L [98].

Among the 44 patients who had normal sodium level on admission, 12 developed hyponatremia during hospital course. This comes to 22.2% compared to 19.9% in the previous study. Sodium level was less than 130 mEq/litre in three patients (5.5%).

Two of them died with in 30 days in hyponatremia developing after admissions. This is 0.8% less than what Goldberg et. al., found in this study [97].

THROMBOLYSIS AND HYPONATREMIA

In Hyponatremia on admission group 50% of them are thrombolysed where as 41.6% only thrombolysed in hyponatremia developed after admission. Among the 3 death in hyponatremia on admission group 2 are thrombolysed.

SEX AND HYPONATREMIA

Among total 54 patients ,40 are males. The remaining 14 are females.

The 3 patients died in hyponatremia on admission group, all are having anterior wall infarction. Two of them showed persistently hyponatremia in the course. Kerry L.Lee., found high mortality rate in anterior wall MI patients [49]

Among the two patients who died in hyponatremia developed after admission group, anterior and inferior wall MI shares 50%. Those who developed hyponatremia after admission only 41.6% of them received diuretic therapy.

RISK FACTORS AND HYPONATREMIA

Hyponatremia is more common in diabetes mellitus, smoker and alocohol patients. Similar results found in the previous study. Diabetes smoker alocholic patients are more prone to develop hyponatremia after admission.

KILLIP CLASSIFICATION AND HYPONATREMIA

Goldberg et. al., found higher killip classification are more prone to develop hyponatremia[97]. In our study hyponatremia on admission is more common in Class I and hyponatremia develped after admission is more common in Class II. This may be due to higher killip class (III, IV) patients makes only 9.2% in our study. General prevalence of killip Class III, IV are 10 -15, 5 -10 respectively[99].

Kerry L.Lee., Eric J Topal found the prevalence of killip class - III, IV is two persent in their study. Even though few patients in killip class III, IV their mortality rate was very high in their study.[49]

DISCUSSION

A 54 patients in this study were all chosen with strict adherence to the entry criteria. Most patients arrived at the hospital without prior referrence by Doctor. Though some study have reported a difference in mortality depending on the qualification of referring Doctor.Our referred cases were too few in number to arrive such a conclusion. 30% of patients are only referred by private practitioners.

In our study the overall mortality rate within 30 days is 12.9% Kerry L.Lee., found that mortality rate within 30 days is 7% in his study, among them 39% died within 24 hours. Alexander Goldberg found 10% mortality within 30 days following MI.

Many studies report the commonest location of MI is anterior infarction, as in our study (27 out of 54 patients). Mortality was also higher in patients with anterior infarction compared to inferior infarction (85.7% Vs. 14.3%). Multiple previous studies have reported that patients with anterior infarction have the highest risk of death[102.103], and isolated inferior infarction has been associated with the lowest risk.

An increasing age has been found to worsen prognosis both in terms of likelyhood of death and in the development of life threatening complications [83] Age over 60 significantly increasing mortality compared to those less than 60 years. The relation was relatively flat until age 60, after which the risk of death accelerated dramatically.

In our study the percentage of mortality in males is more than females. Kerry L.Lee., found female sex was only a marginally independent Prognostic factor (P=0.043) in his study[49].

HYPONATREMIA

In our study hyponatremia was present in 10 out of 54 patients. It comes to 18.5%. Comparing to Goldberg et. al., this is 5.6% higher than what he found. None of them presented with hyponatremia receive prior diuretic therapy. Among hyponatremia on admission the mortality rate is 30%. Goldberg et. al., found 19.9% mortality in hyponatremic patients on admission [97].

In a study of 235 patients admitted to a coronary care unit in the prethrombolytic era (of whom 190 were subsequently diagnosed with acute myocardial infarction), Flear et. al., found higher in-hospital

mortality rates among patients with minimal plasma sodium levels ≤ 130 mmol/L [98].

Among the 44 patients who had normal sodium level on admission, 12 developed hyponatremia during hospital course. This comes to 22.2% compared to 19.9% in the previous study. Sodium level was less than 130 mEq/litre in three patients (5.5%).

Two of them died with in 30 days in hyponatremia developing after admissions. This is 0.8% less than what Goldberg et. al., found in this study [97].

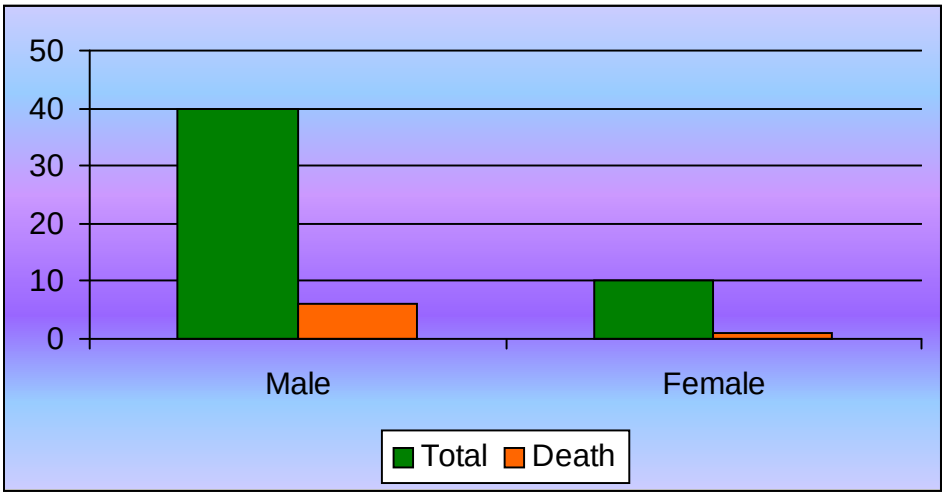
THROMBOLYSIS AND HYPONATREMIA

In Hyponatremia on admission group 50% of them are thrombolysed where as 41.6% only thrombolysed in hyponatremia developed after admission. Among the 3 death in hyponatremia on admission group 2 are thrombolysed.

SEX AND HYPONATREMIA

Among total 54 patients ,40 are males. The remaining 14 are females.

OUTCOME IN MALE AND FEMALE



The 3 patients died in hyponatremia on admission group, all are having anterior wall infarction. Two of them showed persistently hyponatremia in the course. Kerry L.Lee., found high mortality rate in anterior wall MI patients [49]

Among the two patients who died in hyponatremia developed after admission group, anterior and inferior wall MI shares 50%. Those who developed hyponatremia after admission only 41.6% of them received diuretic therapy.

RISK FACTORS AND HYPONATREMIA

Hyponatremia is more common in diabetes mellitus, smoker and alocohol patients. Similar results found in the previous study. Diabetes smoker alocholic patients are more prone to develop hyponatremia after admission.

KILLIP CLASSIFICATION AND HYPONATREMIA

Goldberg et. al., found higher killip classification are more prone to develop hyponatremia[97]. In our study hyponatremia on admission is more

common in Class I and hyponatremia develped after admission is more common in Class II. This may be due to higher killip class (III, IV) patients makes only 9.2% in our study. General prevalence of killip Class III, IV are 10 -15, 5 -10 respectively [99].

Kerry L.Lee., Eric J Topal found the prevalence of killip class - III, IV is two persent in their study. Even though few patients in killip class III, IV their mortality rate was very high in their study.[49]

BIBLOGRAPHY

1. Price FW (Ed); A textbook of the practice of medicine p.1068, 8-th edition, *Oxford University Press*, 1950.

2. Sleight P :"Myocardial infarction" : in Oxford textbook of medicine, vol.II .,p 2331-49, 3 rd edition.,Oxford university press,1996

3. Kennedy JW, Martin GV, Davis KB, Maynard C, Stadius M, Sheehan FH, Ritchie JL. The Western Washington Intravenous Streptokinase in Acute Myocardial Infarction Randomized Trial. Circulation. 1988;77:345-352.

4. Gruppo Italiano per lo Studio della Streptochinasi Nell-Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet. 1986;1:397-401.

5. ISIS-2 Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 casesof suspected acute myocardial infarction: ISIS-2. Lancet. 1988;2:349-360.

6. Wilcox RG, von der Lippe G, Olsson CB, Jensen G, Skene AM, Hampton JR. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction: Anglo-Scandinavian Study of Early Thrombolysis (ASSET). Lancet. 1988;2:525-530.

7. The AIMS Trial Study Group. Effect of intravenous APSAC on mortality after acute myocardial infarction. Lancet. 1988;1:545-549

8. Topol EJ, Califf RM, George BS, Kereiakes DJ, Abbottsmith CW, Candela RJ, Lee KL, Pitt B, Stack RS, O'Neill WW, for the Thrombolysisand Angioplasty in Myocardial Infarction (TAMI) Study Group. A randomized trial of immediate versus
delayed elective angioplasty after intravenous tissue plasminogen activator in acute myocardial infarction. N Engl J Med. 1987;317:581-588.

9. The TIMI Research Group. Immediate versus delayed catheterization and angioplasty following thrombolytic therapy for acute myocardial infarction. JAMA. 1988;260:2849-2858.

10. Weaver WD, Cerqueira M, Hallstrom AP, Litwin PE, Martin JS, Kudenchuk PJ, Eisenberg M. Prehospital-initiated versus hospital-initiatedthrombolytic therapy: the Myocardial Infarction Triage and Intervention Trial. JAMA. 1993;270:1211-1216.]

11. Grines CL, Browne KF, Marco J, Rothbaum D, Stone GW, O'Keefe J, Overlie P, Donohue B, Chelliah N, Timmis GC, Vlietstra RE, Strzelecki M, Puchrowicz-Ochocki S, O'Neill WW, for the Primary Angioplasty in Myocardial Infarction Study Group. A comparison of immediateangioplasty with thrombolytic therapy for acute myocardial infarction. N Engl J Med. 1993;328:673-679.

12. White HD, Norris RM, Brown MA, Takayama M, Maslowski A, Bass NM, Ormiston JA, Whitlock T. Effect of intravenous streptokinase on left ventricular function and early survival after acute myocardial infarction. N Engl J Med. 1987;317:850-855.

13. Brunwald text book of cardiology 7th edi.p 1142,1143

14. Killip T & Kimball JT : Treatment of Myocardial Infarction in a Coronary Care Unit --- A Two Year Experience with 250 Patients. Am. J. Cardiol. 20 : 457, 1967.

15. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico. GISSI-2: a factorial randomised trial of alteplase versus streptokinas and heparin versus no heparin among 12 490 patients with acute myocardial infarction. Lancet. 1990;336:65-71.

16. The International Study Group. In-hospital mortality and clinical course of 20,891 patients with suspected acute myocardial infarction randomised between alteplase and streptokinase with or without heparin. Lancet. 1990;336:71-79.

17. ISIS-3 (Third International Study of Infarct Survival) Collaborative Group. ISIS-3: a randomised comparison of streptokinase vs. tissue plasminogen activator vs. anistreplase and of aspirin plus heparin vs. aspirin alone among 41,299 cases of suspected acute myocardial infarction. Lancet. 1993;339:753-770.

18. The GUSTO-I Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med. 1993;329:673-682.

19. Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT0-3 Investigators : Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin; The ASSENT-randomised trial in acute myocardial infarction. Lancet 358; 605, 2001.

20. Canto JG, Rogers WJ, Chandra NC, et. al., : The association of sex and payer status on management and subsequent survival in acute myocardial infarction. *Arch Intern Med. 162* : 587, 2002.

21. .Sanz G, Castaner A, Betriu A, Magrina J, Roig E, Coll S, Pare JC, Navarra-Lopez F. Determinants of prognosis in survivors of myocardial infarction. N Engl J Med. 1982;306:1065-1070.

22. Norris RM, Brandt PWT, Caughey DE, Lee AJ, Scott PJ. A new coronary prognostic index. Lancet. 1969;1:274-278.

23. Moss AJ, DeCamilla J, Davis H, Bayer L. The early posthospital phase of myocardial infarction: prognostic stratification. Circulation.1976;54:58-64.

24. The Multicenter Postinfarction Research Group. Risk stratification and survival after myocardial infarction from the Multicenter Post-InfarctionResearch Group. N Engl J Med. 1983;309:331-336

25. Dubois C, Pierard LA, Albert A, Smeets J-P, Demoulin J-C, Boland J, Kulbertus HE. Short-term risk stratification at admission based on simple clinical data in acute myocardial infarction. Am J Cardiol. 1988;61:216-219.

26. Hillis DK, Forman S, Braunwald E, for the Thrombolysis in Myocardial Infarction (TIMI) Phase II Coinvestigators. Risk stratification before thrombolytic therapy in patients with acute myocardial infarction. J Am Coll Cardiol. 1990;16:313-315.

27. Mueller HS, Cohen LS, Braunwald E, Forman S, Feit F, Ross A, Schweiger M, Cabin H, Davison R, Miller D, Solomon R, Knatterud GL, for the TIMI Investigators. Predictors of early morbidity and mortality after thrombolytic therapy of acute myocardial infarction: analyses of patient subgroups in the Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase II. Circulation. 1992;85:1254-1264.]

28. Maynard C, Weaver D, Litwin PE, Martin JS, Kudenchuk PJ, Dewhurst TA, Eisenberg MS, Hallstrom AP, Chambers J, for the MITI Project Investigators. Hospital mortality in acute myocardial infarction in the era of reperfusion therapy (the Myocardial Infarction Triage and Intervention Project). Am J Cardiol. 1993;72:877-882.

29. Volpi A, DeVita C, Franzosi MG, Geraci E, Maggioni AP, Mauri F, Negri E, Santoro E, Tavazzi L, Tognoni G, for the Ad hoc Working Groupof the Gruppo Italiano per lo Studio della Sopravvivenza nell-Infarto Miocardico (GISSI-2) Data Base. Determinants of 6-month mortality in survivors of myocardial infarction after thrombolysis: results of the GISSI-2 data base. Circulation. 1993;88:416-429.

30. Braunwald textbook of cardiology 7 th edition p.1142

31. Pasternak RC, E. Braunwald & BE Sobel : "Acute Myocardial Infarction", in Heart Disease : A Textbook of Cardiovascular Medicine., Vol. II, 4-th Edn., WB Saunders.

32. Bean WB : Masquerade of Myocardial Infarction : Lancet. 1 : 1044, 1977.

33. Uretsky et al :Symptomatic acute myocardial infarction with out chest pain :prevalence and clinical course, Am.J.Cardiol. 40:498, 1947

34. Edwards, Bouchier, Haslett & Chilvers (Ed.) : 'Davidson's Principles and Practice of Medicine'; 17-th Edn. ELBS, 1995.

35. Kitchin AH & Pocock SJ : Prognosis of patients admitted to hospital with Acute Myocardial Infarction -- Survival in hospital; Br. Heart J. 39 : 1163-66, 1977.

36. International Study of Infarct Survival (ISIS) - 2 : Colloborative Group; Lancet 2 : 349-60, 1988.

37.Reitt et. al., : Relationship between symptom duration and final infarct size. Circln. 93(1) : 48-53, 1996.

38.. Julian DC : Time as a factor in thrombolytic therapy. Int. J. Cardiol. 49-S : 517-9, 1995

39. Rapaport E: ISIS -3:A critical analysis of the premilinary results .J Myocard Ichemia 3: 25-32 , 1991

40. Paul SD et. al., : Geriatric patients with Acute Myocardial Infarction Am Heart J. 13(14) : 710-5, 1996.

41. Demirovic J et. al., : Sex differences in early mortality after Acute Myocardial Infarction (the Minnesota Heart Survey). Am J Cardiol. 75(16) : 1096-101, 1995.

42. Pamela S Douglas : “Coronary Arterial Disease in Women” in Heart Disease - A Textbook of Cardiovascular Medicine, (Braunwald E Ed.) Vol. II, pp 1704-11; 5-th Edn., Prism-Saunders, 1996.

43. Roberts R et al :pathophysiology ,recognition and treatment of acute myocardial infarction and its complication. Hurst ‘s The Heart , 8 th edn. p 1107-85 , 1994 44. Kodama K et al ;prognostic significance of diadetes mallitus in patients with acute myocardial infarction after recanalisation.diabetes Res clin Pract 30 (suppl) :71-75, 1996.

44. Kodama K et al ;prognostic significance of diadetes mallitus in patients with acute myocardial infarction after recanalisation.diabetes Res clin Pract 30 (suppl) :71-75, 1996

45. Ceremuzynski L : Hormonal and metabolic reactions evoked by acute myocardial infarction. Circulation Res. 48 : 767, 1981.

46. Sack MN, Yellon DM : Insulin therapy as an adjunct to reperfusion after acute com ischemia : A proposed direct myocardial cell survival effect independent of modulation. J Am Coll.Cardiol 41 : 1404, 2003.

47. Fresco C et. al., : Prognostic value of hypertension in11, 483 patients with Acute Myocardial Infarction treatedwith thrombolysis GISSI-2 investigators. J Hypertension 14(6) : 743-50, 1996.

48. Sahreiben et. al., : Cardiologist versus internist management of patients with unstable angina -- treatment patterns and outcomes. J Am Coll Cardiol. 26 (3) : 577-82, 1995.

49. Kerry L. Lee, PhD; Lynn H. Woodlief, MS; Eric J. Topol, MD Predictors of 30-Day Mortality in the Era of Reperfusion for Acute Myocardial Infarction Circulation. 1995;91:1659-1668

50. Crimm A, . Prognostic significance of isolated sinus tachycardia during first three days of acute myocardial infarction. Am J Med. 1984;73:983-988.

51. Disegni et. al., : The predictive value of admission heart rate on mortality in Acute Myocardial Infarction - The SPRINT Study Group. J. Clin Epidemiol. 48 : (10) 1197-205, 1996.

52. Hands ME et. al., : Incidence, predictors and outcome after the in-hospital development of cardiogenic shock after Acute Myocardial Infarction. J Am Col. Cardiol. 14 : 40-6, 1989.

53. Sabatine MS, Morrow DA, Cannon CP, et. al., :
Relationship between baseline white blood cell count and degree of coronary artery disease and mortality in patients with coronary syndromes : A TACTICS-TIMI 18 (Treat Angina with Aggrastat and deter. Cost of Therapy with an Invasive or Conservative Strategy-Thrombolys Myocardial Infarction 18 trial) substudy. J AM Coll. Cardiol 40 : 1761, 2002.

54. Brron HV, Cannon CP. Murphy S.A. et. al., :
Association between white blood cell count, epicardial blood flow, myocardial perfusion, and clinical outcomes in the setting of acute myocardial infarction : A thrombolysis in myocardial infarction 10 substudy. Circulation 102 : 2329, 2000.

55. Furman et. al., : Effect of elevated leucocyte count on in-hospital mortality following Acute Myocardial Infarction.
Am J. Cardiol 78(8) : 945-8, 1996.

56. Petrov D. et. al., : The prognositc significance of high leucocyte count in Acute Myocardial Infarction. Vutr. Boles. 29 (1) : 56-8, 1990.

57. Bellodi G. et. al., : Hyperglycemia and prognosis of Acute Myocardial Infarction in patients without diabetes. J. Am Coll. Cardiol 64 : 885, 1989.

58.. Datey KK et. al., : Hyperglycemia after Acute Myocardial Infarction. NEJM. 276 : 262, 1976.

59, Anderson RJ, Chung HM, Kluge R, Schrier RW. Hyponatremia : A prospective analysis of its epidemiology and he pathogenetic role of vasopressin. Ann Intern Med. 1985; 102 : 164 - 168.

60. Chung HM, Kluge R, Schrier RW, Anderson RJ. Postoperative hyponatremia. A prospective study. Arch Intern Med. 1986; 146 : 333 - 336.

61 Schrier RW. Body fluid volume regulation in health and disease : a unifying hypothesis. Ann Intern Med. 1990;113 : 155 - 159.

62 Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. N.E igl J Med. 1999; 341 : 577 - 585.

63 Kleinfeld M, Casimir M, Borra S. Hyponatremia as observed in a chronic disease facility. J Am Geriatr Soc. 1979; 27: 156 - 161.

64. CMDT 2006 , P 866

65. Gennari FJ.Hypo-hypernatraemia:disorders of water balance.In:Davidson AM,Cameron JS,Grünfeld J-P,Kerr DNS,Ritz E,Winearls CG,eds. Oxford textbook of clinical nephrology.
2nd ed.Vol.1.Oxford,England: Oxford University Pr ess,1998:175-200.

66 . Hyponatremia and hypernatremia.In:Adrogué HJ,Wesson DE.Salt&water.Boston:Blackwell Scientific,1994:205-84.

67. Gennari FJ.Serum osmolality :uses and limitation
Engl J Med 1984. 310 .102-5

68. Arieff AI, Llach F, Massry SG. Neurological manifestations and morbidity of hyponatremia: correlation with brain water and electrolytes. Medicine (Baltimore) 1976:55; 121-9

69. Lee WH, Packer M. Prognostic importance of serum
sodium concentration and its modification by converting -enzyme inhibition in patients with severe chronic heart failure.
Circulation. 1986; 73 : 257 - 267.

70. Saxon LA, Stevenson WG, Middlekauff HR, et. al., Predicting death from progressive heart failure secondary to inschemic or idiopathic dilated cardiomyopathy. Am J Cardiol. 1993; 72 : 62 - 65.

71. Hurst ‘s the heart 12th edn vol.1 p 716

72. Rose BD, Post TW. Hypoosmolal states -- hyponatremia. Clinical Physiology of Acid-Base and Electrolyte disorders. New York, New York : McGraw-Hill; 2001 : 696 - 745

73, Schrier RW, Abraham WT.: Hormones and hemodynamics in heart failure, N. Engl. J. Med. 1999; 341 : 577-585

74. Francis GS, Benedict C, Johnstone DE, et. al., : Comparison of neuroendocrine activation in patients with left ventricular dysfunction with and without congestive heart failure. A substudy of the Studies of Left Ventricular Dysfunction (SOLVD). Circulation 1990; 82 : 1724-1729.

75. Goldsmith SR, Francis GS, Cowley AW Jr. et. al., : Increased plasm arginine vasopressin levels in patients with congestive heart failure.J Am Coll. Cardiol 1983; 94 : 3206-3211.

76. Goldsmith SR, Francis GS. Cowley AW Jr, et. al., : Hemodynamic effects of infused arginine vasopressin in congestive heart failure. J Am Coll. Cardiol 1986; 8 779-783.

77. Keeton TK, Campbell WB. : The pharmacologic alteration of renin release. Pharmacol Rev. 1981;31 : 82-227.

78. Schrier RW, Berl T, Anderson RJ. Osmotic and nonosmoticcontrol of vasopressin release. Amj Physiol. 1979;236:F321-332.

79. Kim UK, Michel JB, Soubrier F, et.all., Arginine vasopressin gene expression in chronic cardiac failure in rats Kidney, Int. 1990;38:818-822.

80. Xu DL, Martin PY, Ohara M, et.al., Upregulation of aquaporin-2 water channel expression in chronic heart failure rat. J Clin Invest. 1997;99:1500-1505.

81. Morrow DA, Antman EM, Giugliano RP, et. al., A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction : an In TIME II substudy. Lancet. 2001; 358 : 1571 - 1575.

82. Morrow DA, Antman EM, Charlesworth A, et.al., TIMI risk score for ST-evevation myocardial infarction: a convenient. bedside, clinical score for risk assessment at presentation:an intravenous nPA for treatment o f infarcting myocardium early II trial substudy.
Circulation. 2000; 102:2031-2037

83. Lee KL, Woodlief LH, Topol EJ, et.al., Predictors of 30-day mortality in the era of reperfusion for acute myocardial infaction. Results from an international trial of 41,021 patients. GUSTO-I Investigatiors.
Circulation.1995;91:1659 - 1668.

84. Adrogue HJ, Madas NE. Hyponatremia. N Engl Med. 2000;342:1581-1589.

85 Rowe JW, Shelton RL. Helderman JH, et.al., Influence of the emetic reflex on vasopressin release in man. Kidney int. 1979;16:729-735.

86. Schaller MD, Nussberger J, Feihl F, et.al., Clunical and hemodynamic correlates of elevated plasma arginine vasorpressin after acute myocard al infarctior. Am J Cardiol, 1987;60:1178-1180.

87. Cohn JN, Levine TB, Olivari MT, Et.al., Plasma norepinephrine as a guide to prognosis in patients with chronic congestive heart failure. N Engl J Med1984;311:819-823.

88. Dzau VJ, Colucci WS, Hollenberg NK, Williams GH. relation of the renin-angiotensin-aldosterone system to clinical state in congestive heart failure, Circulation. 1981;63:645-651.

89. Szatalowicz VL, Arnold PE, Chaimovitz C, et. al., Radioimmunoassay of plasma arginine vasopressin in hyponatremic patients with congestive heart failure.. N Engl J Med. 1981; 305 : 263 - 266.

90. Schaer GL, Covit AB, Laragh JH, Cody RJ. Association of hyponatremia with increased renin activity in chronic congestive heart failure impact of diuretic therapy.Am J Cardiol. 1983; 51 : 1635 - 1638.

91. Stein BC, Levin RI : Natriuretic peptides : Physiology, therapeutic potential and stratification in ischemic heart disease. Am Heart J. 135 : 914, 1998.

92. de Lemos JA, Morrow DA, Bentley JH, et. al., : The prognostic value of B-type natriuretic. peptide in patients with acute coronary syndromes. N. Engl. J. Med. 345 : 1014, 2000.

93. Morrow DA, Braunwald E : Future of biomarkers in acute coronary syndromes; Circulation 108 : 250, 2003.

94. Arthur E.Weymen ,Principles and practice of echocardiography. 2 nd edn., Lea & Febiger 1 994

95. Peels et al :LV wall motion score as an early predictor of mortality after first acute myocardial infarction treated with thrombolysis - the CATS investigations group.Am J Cardio. 77 (14):1149-54, 1996

96. Pozzoli et al :Doppler evaluvation and PCWP provide similar Prognostic,information in patients withsystolic dysfunction afer acute myocardial infarction. Am HEART j.129 (4):716-25, 1995

97. **ALEXANDER GOLDBERG, MD, et al**, Prognostic importance of hyponatremia in acute ST ELEVATION myocardial infarction .
A m,J. Med.2004:117: 242-248

98. Flear CT, Hilton P. Hyponatraemia and severity and outcome of myocardial infarction. BMI. 1979; 1 :1242 - 1246.

99. Hurst ‘s the heart 12th edn, vol.2, p 1316

100. Rose BD, Post TW. Hypoosmolal states – hyponatremia In : Clinical Physiology of Acid-Base and Electrolyte Disorders. New York, New York : McGraw-Hill; 2001 : 696 - 745.

101. Katz MA. Hyperglycemia-calculation of expected serum sodium depression. N Engl J Med. 1973; 289 :
843 - 844.

102. Crimm A, Severance HW Jr, Coffey K, McKinnis R, Wagner GS, Califf RM. Prognostic significance of isolated sinus tachycardia during first three days of acute myocardial infarction. Am J Med. 1984;73:983-988.

103. Taylor GJ, Humphries JO, Millits ED, Pitt B, Schulze RA, Griffith LS, Achuff SC. Predictors of clinical course, coronary anatomy and left ventricular function after recovery from acute myocardial infarction. Circulation. 1980;62:960-970.

Hyponatermia in STEMI

								Blood Sugar				Serum Sodium				Serum Pottasiam				LVEF	Diuretic
S.No.	Name	I.P.No.	Age	Sex	Diagnosis	Th	Pre	Adm	24 hr	48 hr	72 hr	Adm	24 hr	48 hr	72 hr	Adm	24 hr	48 hr	72 hr		
1	Ramaiya	860591	45	M	Ext. AWMI	No	DM	158	392	100	208	135	136	136	139	3.5	4.5	3.9	4.3	58%	No
2	Ganapathy	860670	67	M	AWMI	No	S+DM	228	228	184	212	139	136	131	131	4.6	40	4.3	3.9	49%	Yes
3	Balaiyan	860945	60	M	AS,IW MI	No	S+A	140	87	81	104	130	137	130	132	4.7	3.3	50	4.8	30%	No
4	Nagarathinam	860952	85	M	IW,PMI	No	HT	136	108	100	128	135	136	134	126	38	29	3.1	4.5	61%	No
5	Franchis	861073	62	M	IWMI	No	HT,DM	112	158	156	136	135	136	137	135	4.4	5.1	4.4	4.2	58%	No
6	Ganathammal	861226	70	F	ASMI	No	HT	96	128	134	164	132	138	131	134	3.8	3.9	4.1	4.3	50%	No
7	Kannappan	861500	45	M	ASMI	Yes	S+A	100	108	0	0	138	136	0	0	4.4	3.7	4.2	4.4	0	No
8	Thumbuswamy	861493	65	M	ASMI	No	DM	124	140	105	136	138	130	137	132	4.6	4.4	3.9	4.2	62%	Yes
9	Manikandan	861506	38	M	Ext. AWMI	No	S	124	100	75	98	136	128	134	133	3.7	3.7	4	3.9	54%	No
10	Dhatchinamoorthy	862000	45	M	IWMI	No	DM	148	195	325	322	136	140	141	133	3.8	3.9	2.2	3.8	47%	No
11	Mathivanan	862097	45	M	AW,LATMI	No	S+A	123	115	46	80	136	134	138	133	3.9	3.7	3.6	3.7	68%	No
12	Muniyamuthu	862125	64	M	IW,PMI	No	DM,S	210	163	126	140	136	136	137	140	4.1	3.9	4.2	3.8	60%	No
13	Shenbagavalli	862160	55	F	ASMI	No	HT	86	106	108	118	135	139	136	140	4.1	4.3	3.5	3.8	54%	No
14	Seethiammal	862367	60	F	ASMI	No	HT	96	136	135	136	135	135	138	142	4	4.4	4.1	4.2	48%	Yes
15	Jamil	862367	55	M	IW,RVMI*	Yes	DM	217	132	108	170	138	139	138	138	4.2	4.1	4.1	3.9	38%	No
16	Subramaniyan	862481	52	M	IW,PMI	Yes	S+A	100	90	98	104	134	132	139	134	3.9	3.8	3.2	3.6	60%	No
17	Sivagnannam	862105	50	M	IWMI	Yes	HT	110	104	92	256	138	136	139	137	3.9	4.6	4.7	4.1	60%	No
18	Murugaiyan	863589	55	M	AWMI	Yes	DM,HT	101	92	102	96	135	127	136	136	3.9	4.7	4.8	4.2	51%	Yes
19	Manikandan	863825	51	M	IW,PMI	Yes	S+A	103	80	94	86	138	135	140	138	3.7	4.9	4.8	4.1	55%	No
20	Kanagammal	864033	70	F	IWMI	Yes	DM,HT	272	110	134	169	134	138	137	139	4.1	0.3	3.9	4.2	65%	No
21	Murugaiyan	864392	50	M	AWMI	No	DM	134	98	146	130	136	136	138	138	4.2	4.1	4.2	4.2	52%	No
22	Palanivel	869847	50	M	AWMI	Yes	S+A	84	90	106	98	132	133	140	134	4.1	3.9	4.5	5.1	54%	No
23	Dharmalingam	869879	60	M	IW,P,RVMI	Yes	HT	53	60	76	83	136	138	136	137	3.8	3.9	4.2	4.2	60%	No
24	Pannerselvam	869892	38	M	AWMI	Yes	S	120	110	98	116	130	132	136	132	4.3	3.8	3.2	3.6	58%	No
25	Govindasamy	869964	68	M	IW,PMI	No	DM	100	96	108	120	136	136	140	136	4.6	4.2	3.2	3.8	44%	No
26	David	871035	62	M	H.LATMI	No	HT	138	120	116	120	136	136	138	139	3.9	3.8	3.6	3.6	51%	No
27	Govindaraj	871045	70	M	GLOBALMI	Yes	HT	120	108	130	110	136	135	136	136	3.8	4.4	4.2	4.4	60%	No
28	Rajagopal	871084	50	M	IWMI	Yes	DM	180	114	136	148	135	138	142	141	4.3	4.2	4.2	4.3	50%	No
29	Rajmohammed	871209	52	M	IW,PMI	Yes	DM	164	140	180	165	135	135	136	138	4.5	4.2	4.3	4.2	60%	No
30	Jayaraman	872795	68	M	IW,PMI	Yes	HT,DM,S	576	209	228	180	136	131	132	136	3.9	4.6	4.4	4.4	67%	Yes
31	Suresh	872902	35	M	AWMI	No	S+A	68	57	96	86	135	132	136	133	3.7	3.8	3.9	3.9	55%	Yes
32	Elamaran	872993	36	M	IW,PMI	Yes	HT,S,A,DM	433	108	139	108	136	136	132	134	3.6	3	3.9	3.9	41%	No
33	Pappa	872915	55	F	AWMI	Yes	HT	94	98	106	80	139	138	138	139	4.4	3.8	4.1	3.8	64%	No
34	Mangayarkarasi	872583	55	F	PMI	Yes	DM	200	140	140	184	134	132	130	133	4.3	4.1	3.9	3	56%	Yes
35	Elangovan	872451	52	M	IWPMI	Yes	HT,S,A	77	90	108	86	137	138	140	136	4.2	4	4.1	4.1	65%	No
36	Kannapillai	873749	55	M	AWMI	Yes	DM	232	408	276	192	131	135	130	131	4.3	3.8	4.2	4.1	63%	No
37	Rukhmani	875018	52	F	IWPMI	Yes	HT	116	108	96	84	132	136	135	134	4.2	3.8	4.2	4.1	65%	No
38	Meenammal	875261	55	F	AWMI	Yes	HT,S	116	84	110	120	138	136	138	136	3.9	3.9	4	4.1	63%	Yes
39	Jothi	875769	52	F	AWMI	No	HT	120	96	110	98	139	136	141	144	4.3	4.2	4.1	4.2	60%	No
40	Vedarathinam	876094	55	M	AW,I, MI	No	S	79	110	98	76	136	135	136	139	3.9	3.8	4.2	4.2	36%	No
41	Chandramohan	876389	50	M	Ext. AWMI	Yes	HT	80	92	96	118	135	136	136	139	4.7	3.3	5	4.8	62%	No
42	Raja	877244	32	M	AWMI	No	DM,A	144	180	164	160	132	138	140	138	4	4.2	4.2	4.4	44%	No
43	Sekar	877258	40	M	IWMI	Yes	DM,S	140	128	96	138	138	136	136	136	4.3	4.2	4.1	4.3	65%	No
44	Shahul Hameed	878850	62	M	AWMI	No	HT,S	104	110	142	130	135	136	136	138	4.4	4.2	4.1	4.3	65%	Yes
45	Lathika Beevi	878910	60	F	IWMI	Yes	DM	208	148	160	170	136	131	132	132	3.3	3.6	3.2	3.2	61%	No
46	Sivagami	878970	55	F	IW,P,MI	No	HT	111	90	86	84	136	132	136	136	3.8	3.6	3.6	3.2	52%	No
47	Arulanantham	881513	54	M	IWMI	No	DM	124	140	184	164	138	136	138	136	3.4	4.5	4.3	4.2	60%	No
48	Rajalakshmi	881552	50	F	AWMI	No	HT,DM	363	320	280	262	133	136	134	133	4.1	4.2	4.4	4.2	50%	No
49	Murugaiyan	881761	60	M	IWMI	YES	HT,DM	82	110	122	121	131	136	132	132	4.4	4.2	4.2	4.6	50%	No
50	Pattu	881793	70	F	IWMI	NO	DM	92	110	140	118	132	132	132	130	3.7	3.6	3.6	3.8	46%	No
51	selvam	881884	50	M	PWMI	Yes	DM,S	236	240	242	218	140	134	136	138	4.1	4	3.8	3.6	50%	No
52	Rajendran	881904	45	M	AWMI	NO	HT	112	110	110	106	136	140	136	136	4.4	4.2	4.2	4	50%	No
53	kaliyaperumal	882080	45	M	H.LAT.MI	YES	S	119	120	122	136	136	140	138	138	3.7	3.6	3.2	3.2	46%	No
54	Manickam	882125	76	M	IWMI	No	HT	124	184	140	164	136	138	141	136	4.2	4.1	4.1	4	52%	No

ABBREVIATIONS FOR MASTER CHART

Thy– thrombolysis,

Pre- previous history of DM, HT etc

DM-diabetes mellitus

HT-hypertension

S-smoker

A-alcohol habits

Adm- admission

AWMI -anterior wall myocardial infarction

ASMI –antero septel myocardial infarction

Ext,AWMI-extencive anterior wall myocardial infarction

IWMI- inferior wall myocardial infarction

P – posterior

RV-right ventricular infarction

N -no

Y-yes

Pulse –pulse rate / min

T.C.-total count

Hb.-haemoglobin

LVEF-left ventricular ejection fraction

A-alive

D-died

HYPONATREMIA IN ACUTE STEMI

NAME : Age: years. Sex: male/female
Occupation I.P.NO:
ADDRESS : D.O.A:
D.O.D:

Phone:
DATE & TIME OF ONSET OF PAIN:

DATE & TIME OF ADMISSION :

SYMPTOMS: ☐ CHEST PAIN / ☐ DYSPNOEA / ☐SWEATING /☐GIDDINESS

RISK FACTORS: DIABETES MELLITUS TYPE 1 TYPE 2 YEARS
HYPERTENSIVE YEARS
SMOKER YEARS
ALCOHOLIC YEARS
FAMILY HISTORY : DM/ HT/ CAHD

FINAL DIAGNOSIS :

KILLIP CLASSIFICATION: I / II / III / IV

☐ THROMBOLYSED /☐ NOT THROMBOLYSED

DIURETIC THERAPY : ☐ YES / ☐NO

☐ PREVIOUS / ☐STARTED

DAY	ADMISSION	DAY 2	DAY 3	DAY 4
Pulse / min				
B.P. mmHg				
Basal Crepts				
C.V.S.				

INVESTIGATIONS:

URINE : BLOOD : Hb: T.C :
ALBUMIN: D.C: P. % L. % E. %
REDUCING SUBSTANCE : R.B.C:

BLOOD UREA : mgs/dl SERUM CREATININE : mgs/dl

ELECTRO CARDIO GRAPHIC FINDINGS :

DATE /DAY					
RATE /MIN					
RHYTHM					
PR INTERAL					
QRS COMPLEX					
ST SEGMENT					
T WAVE					
BLOCK					

DAY	ADMISSION	24 HOURS	48 HOURS	72 HOURS
Bl.sugar mgs%				
Serum Na mEq/l				
Corrected Na mEq/l				
Serum K mEq/l				

ECHO CARDIO GRAPHIC FINDINGS :

CAHD- HYPOKINESIA OF ANTERIOR WALL

LOWER ½ IVS

INFERIOR WALL

L V E F : %

OUTCOME IN 30 DAYS : ☐ ALIVE ☐ DEATH